

PATENT

Application No.: 09/724,571
Page 4

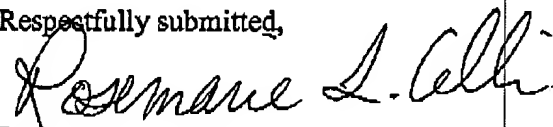
and 132 read on SEVNLD AEF (SEQ ID NO: 83). Applicants request that the Examiner acknowledges claims 78 and 133 as generic.

Sequence Election Requirement

Applicants traverse the sequence election requirement. The requirement is moot as to the claims under consideration in the instant application. The sequence election requirement only applies to claims drawn to amino acid sequences, and does not apply to the claims of group elected in the instant application, Group V. The Office Action states, "[f]or an elected Group drawn to amino acid sequences, the Applicants must further elect a single amino acid sequence." (Emphasis found in the original). (See page 8, ¶1 of the Office Action mailed January 17, 2002). The claims of Group V are drawn to a method for screening, not amino acid sequences. (See page 2, ¶6 of the Office Action mailed January 17, 2002). Based on the foregoing, the sequence election requirement is moot.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,


Rosemarie L. Celli
Reg. No. 42,397

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (650) 326-2400
Fax: (650) 326-2422
RLC:lah
PA 3249309 v1

PATENT

Application No.: 09/724,571
Page 5

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend the claims as follows.

78. (Amended) A method of screening for compounds that inhibit A β production, comprising contacting a[an isolated] β -secretase polypeptide purified to apparent homogeneity comprising a polypeptide that (i) is fewer than about 450 amino acid residues in length, (ii) includes an amino acid sequence that is at least 90% identical to SEQ ID NO: 75 including conservative substitutions thereof, and (iii) exhibits β -secretase activity, as evidenced by an ability to cleave a substrate selected from the group consisting of the 695 amino acid isotype of beta amyloid precursor protein (β APP) between amino acids 596 and 597 thereof, MBP-C125wt (SEQ ID NO: 103) and MBP-C125sw (SEQ ID NO: 104)[according to claim 37] with (i) a test compound and (ii) a β -secretase substrate, and selecting the test compound as capable of inhibiting A β production if said β -secretase polypeptide exhibits less β -secretase activity in the presence of said compound than in the absence of said compound.

81. (Amended) The method of claim 78, which further includes administering said test compound to a mammalian subject having a condition characterized by A β peptide amyloid deposits[Alzheimer's disease or Alzheimer's disease-like pathology], and selecting said compound as a therapeutic agent candidate if, following such administration, said subject maintains or improves cognitive ability or said subject shows reduced plaque burden.

84. (Amended) The method of claim 78, wherein said β -secretase substrate is selected from the group consisting of MBP-C125wt (SEQ ID NO: 103), MBP-C125sw (SEQ ID NO: 104), APP, APPsw, and β -secretase-cleavable fragments thereof.

85. (Amended) The method of claim 78, wherein said β -secretase[-cleavable fragment]substrate has a sequence selected from the group consisting of SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94, SEQ ID NO: 95, and SEQ ID NO: 96.

PATENT

Application No.: 09/724,571
Page 6

132. (New) The method of claim 78, wherein the β -secretase substrate has a sequence selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 78, and, SEQ ID NO: 81, and, SEQ ID NO: 97, and selecting the test compound as capable of inhibiting A β production if said β -secretase polypeptide exhibits less β -secretase activity in the presence of the test compound than in the absence of the test compound.

133. (New) A method of screening for compounds that inhibit A β production, comprising contacting an isolated β -secretase comprising a polypeptide that (i) is fewer than about 450 amino acid residues in length, (ii) includes an amino acid sequence that is at least 90% identical to SEQ ID NO: 75 including conservative substitutions thereof, and (iii) exhibits β -secretase activity, as evidenced by an ability to cleave a substrate selected from the group consisting of the 695 amino acid isotype of beta amyloid precursor protein (β APP) between amino acids 596 and 597 thereof, MBP-C125wt (SEQ ID NO: 103) and MBP-C125sw (SEQ ID NO: 104) with (i) a test compound and (ii) a β -secretase substrate, wherein the β -secretase substrate is an inhibitor of β -secretase activity.

134. (New) The method of claim 133, wherein the β -secretase substrate has a sequence selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 78, and, SEQ ID NO: 81, and, SEQ ID NO: 97, and selecting the test compound as capable of inhibiting A β production if said β -secretase polypeptide exhibits less β -secretase activity in the presence of the test compound than in the absence of the test compound.

PA 3249309 v1